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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/610,551	07/05/00	BARBAS C	TSRI 409.1D2

HM12/0226
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EXAMINER	
TUNG, M	
ART UNIT	**PAPER NUMBER**
1644	6

DATE MAILED: 02/26/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/610,551	Applicant(s) Barbas, et al.
	Examiner Mary B. Tung	Group Art Unit 1644

☒ Responsive to communication(s) filed on *Dec 4, 2000*

☐ This action is **FINAL**..

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1, 4, 5, 8, 11, 12, and 14-34* is/are pending in the applicat

Of the above, claim(s) *1, 4, 5, 8, 11, and 12* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *14-34* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *1 and 4*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Applicant's election, without traverse, of Group II, claims 14-34 in the paper filed Dec. 4, 2000, Paper No. 5 is acknowledged.

2. Group I, claims 1, 4, 5, 8, 11 and 12 are withdrawn from further consideration by the Examiner, 37 C.F.R. 1.142(b), as being drawn to non-elected inventions.

3. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with *37 C.F.R. § 1.48(b)* if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under *37 C.F.R. § 1.48(b)* and by the fee required under *37 C.F.R. § 1.17(h)*.

Priority

4. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

5. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 C.F.R. 1.78). Reference to parent applications 09/300,386 and 08/931,645 must be included in the first sentence of the specification.

Information Disclosure Statement

6. The information disclosure statement filed fails to comply with 37 C.F.R. 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The reference lined through on the PTO Form 1449, filed 11/3/2000 was not considered by the Examiner because the reference was not provided to the office and was not available in the parent cases.

7. Some of the references cited in the in information disclosure statement filed 11/3/2000, have not been considered, and will not be listed on any patent resulting from this application because they were not provided on a separate list with the instant application. In order to have the references printed on such resulting patent, a separate listing, preferably on a PTO-1449 form, must be filed. Those references that were listed on a PTO-1449 have been considered by the Examiner.

Specification

8. The use of the trademarks such as "pBLUESCRIPT," page 42, lines 9 and 15, "TAQ," page 46, line 12, "GENEAMP," page 46, line 16, "MICROTITER" page 71, lines 2 and 3, "BIACORE" page 75, lines 31 and 35, and so on, of the specification has been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

9. Each letter of the trademarks must be capitalized. *See MPEP 608.01(V)* and *Appendix 1.*

Claim Rejections - 35 U.S.C. § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 22 and 32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

12. It is apparent that hybridoma (ATCC Accession Number 75408) is required to practice the claimed invention. The reproduction of an identical cell line is an extremely unpredictable event. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. The instant specification does not disclose a repeatable process to obtain the hybridomas and it is not apparent if the hybridomas are readily available to the public. If it is not so obtainable or available, the enablement requirements of *35 U.S.C. 112*, first paragraph, may be satisfied by a deposit of said hybridoma. *See 37 C.F.R. 1.802*. It is noted that the Applicants have disclosed on page 10 that the cell line was deposited with ATCC on Feb. 2, 1993, under terms of the Budapest Treaty.

13. If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating

that the deposit has been made under the terms of the Budapest Treaty and that **all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent**, would satisfy the deposit requirements. *See 37 C.F.R. 1.808.*

14. In addition, the identifying information set forth in *37 C.F.R. 1.809 (d)* should be added to the specification. *See 37 C.F.R. 1.803-1.809* for additional explanation of these requirements, Amendment of the specification to disclose the date of deposit and the complete name and address of the depository is required (ATCC, 10801 University Boulevard, Manassas, VA 20110-2209) on pages 34, line 25 and page 90, line 16.

15. If the deposit was made after the effective filing date of the application for a patent in the United States, a verified statement is required from a person in a position to corroborate that the plasmid described in the specification as filed are the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from Applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the Applicant's possession at the time the application was filed.

16. Applicant's attention is directed to *In re Lundak*, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985), and 37 C.F.R. 1.801-1.809 for further information concerning deposit practice.

Claim Rejections - 35 U.S.C. § 112

17. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his invention.

18. Claims 14-22 and 25-32 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: steps by which the PCR-amplified nucleotide sequences are used to produce an antibody, is not recited in the claims. Recitation of steps, such as recited in claims 23, 24, 33 and 34 would help to overcome this rejection.

19. Claims 14-34 are rejected under *35 U.S.C. § 112*, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

20. Claims 14 and 25 recite the limitation "framework region". Lacking a clear definition of said limitation in the specification, it is unclear to which sequences the Applicants intend the claims to encompass.

Claim Rejections - 35 U.S.C. § 103

21. The following is a quotation of *35 U.S.C. § 103* which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under *subsection (f) or (g)* of *section 102* of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

22. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

23. Claims 14, 17-19, 25 and 28-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cumano and Rajewsky *(EMBO J 5(10):2459-2468, 1986)* in view of Higuchi *(Using PCR to Engineer DNA, in: PCR Technology, Erlich, HA, ed. Stockton Press, New York, pp. 61-70, 1989).*

24. Cumano and Rajewsky teaches a method for producing an antibody combining site (equivalent to the V_H site) oligonucleotides having 3' and 5' termini comprising a nucleotide sequence at said 3' terminus capable of hybridizing to a first framework region of an immunoglobulin gene; a nucleotide sequence at said 5' terminus capable of hybridizing to a second framework region of an immunoglobulin; and a nucleotide sequence between said 3' and 5' termini according to the formula: $[NNK]_n$, wherein N in independently any nucleotide, K is G or T, n is 10 ; said 3' and 5' terminal nucleotide sequences having a length of about 6-50 nucleotides (see Fig. 1, Vλ1 and homologous sequences, nucleotide codon #25-29, page 2461 and Fig. 2, V186.2 and homologous sequences, nucleotide codon #50-59, page 2462) and wherein the CDR is CDR3, as recited in claims 19 and 30 (see the abstract). Claims 14 and 20 are included because the nucleotide sequence according to the formula $[MNN]_n$, wherein N is independently any nucleotide, M is A or C, is the complement of the sequence $[NNK]_n$,

which meets the limitation of claims 14 and 25 of any complementary sequences. Additionally, the complementary sequence is inherent in any DNA sequence. Also, in the absence of a clear definition of "framework region" in the specification, the Examiner has assumed the definition to include any non-CDR region (see page 19, lines 9-16, of the specification for example). Therefore, the nucleotide sequences at the 5' and 3' (JH) regions would meet the limitations of the claims. The claimed invention differs from the reference teaching only by the recitation of the method using PCR and the antibodies being human, as recited in claims 18 and 29. However, Higuchi teaches that using PCR for the introduction of DNA alterations via the PCR primers is of great utility. Higuchi also teaches the PCR can be used to help create DNA fragments altered in sequence at any position in, or to recombine DNA sequences at any desired junction. (see page 62). One of ordinary skill in the art at the time the invention was made would have been motivated to use the PCR method taught by Higuchi in a method of making a mutated antibody, as taught by Cumano and Rajewsky. Also, one of ordinary skill in the art would have recognized that using human antibodies would reduce the immune response to antibodies derived from other animal species. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

25. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

26. Papers related to this application may be submitted to Group 1640 by facsimile transmission. Papers should be faxed to Group 1640 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). THE CM1 FAX CENTER TELEPHONE NUMBER IS (703) 305-3014 or (703) 308-4242.

27. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Mary Tung whose telephone number is (703)308-9344. The Examiner can normally be reached Tuesday through Friday from 8:30 am to 6:00 pm and on alternating Mondays. A message may be left on the Examiner's voice mail service. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any

inquiry of a general nature or relating to the status of this application should be directed to the Group 1640 receptionist whose telephone number is (703) 308-0196.

February 25, 2001
Mary B. Tung, Ph.D.
Patent Examiner
Group 1640

MARY BETH TUNG, PH.D
PATENT EXAMINER